Case report

Tamoxifen for retroperitoneal fibrosis

JC Chambers Macmillan Consultant and Medical Director, Katharine House Hospice, East End, Adderbury, Oxon and K McGovern Lymphoedema Nurse Specialist, Katharine House Hospice, East End, Adderbury, Oxon

Retroperitoneal fibrosis is characterised by diffuse inflammatory proliferation of fibroblasts and the deposition of collagen fibrils throughout the retroperitoneum, especially in perivascular sites. This results in blockage of the ureters and other tubular retroperitoneal structures such as the vasculature and lymphatic channels. Left untreated, it typically follows a progressive and fatal course. The condition responds favourably to tamoxifen and several case reports describe an improvement in renal function on this therapy. This case report describes a subjective and objective functional improvement of lymphoedema secondary to retroperitoneal fibrosis with the use of tamoxifen. 

Key words: fibroblast; lymphoedema; retroperitoneal fibrosis; tamoxifen

Introduction

Retroperitoneal fibrosis (RF) is a rare condition that was first described in 1948, typically affecting males in the fifth decade. It is characterised by diffuse inflammatory proliferation of fibroblasts and the deposition of collagen fibrils throughout the retroperitoneum, especially in perivascular sites. This results in blockage of the ureters and other tubular retroperitoneal structures such as the vasculature and lymphatic channels. It can also invade local intraperitoneal structures such as the common bile duct and intestine, but it does not metastasise. Typical symptoms include those of renal impairment, subacute intestinal obstruction and lymphoedema. Spontaneous regression of this histologically benign condition is very rare, and it typically follows a progressive and potentially fatal course.

In a review of 481 cases, 68% were idiopathic, 12% were due to methylsergide exposure and 8% were associated with malignancy. Less common aetiological factors included trauma and a diverse range of systemic fibroses and chronic inflammatory processes. Diagnosis is confirmed by biopsy of a suspicious retroperitoneal mass or the radiological finding of hydronephrosis with medial deviation of a tortuous and extrinsically compressed ureter.

Several treatments, including debulking and bypass surgery, corticosteroids, antibiotics, chemotherapy and radiation therapy, have proven unhelpful. However, following successful management of desmoid tumours with tamoxifen, two patients whose RF responded favourably to this drug were described in 1991. There were several subsequent reports of patients with RF whose ureteric stents were permanently removed once established on tamoxifen.

We describe the successful management with tamoxifen of a man who presented to the lymphoedema service with RF.

Case history

A 51-year-old man with carcinoma of the sigmoid colon and left hydronephrosis received chemoradiotherapy before undergoing a sigmoid colectomy and left nephroureterectomy. Histology demonstrated a T4N0M0 adenocarcinoma of the colon that had infiltrated the adjacent small intestine, and a chronic inflammatory process in the left renal system. The primary cancer was completely excised. One year later, a right ureteric stent successfully reversed a rising creatinine level due to the development of a right hydronephrosis. He received a radiological diagnosis of RF, subsequently developing external compression of the inferior vena cava that became barely patent. A magnetic resonance venogram also demonstrated a thrombosed left common iliac vein and external compression of the right iliac system, but...
there was no evidence of cancer recurrence. He was considered too unwell for inferior vena cava stent insertion.

When referred for lymphoedema management, he had massive oedema from the mid-chest down, including genital oedema and lipodermatosclerosis of both legs. He suffered frequent episodes of cellulitis. There was pronounced cutaneous collateral circulation. He could barely bend his hips or knees and became severely dyspnoeic on minimal exertion. Leg volumes were 10421 mL on the left and 9991 mL on the right.

Compression hosiery exacerbated the truncal oedema intolerably. Sequential pump therapy and manual lymphatic drainage were of partial functional benefit. The addition of oral tamoxifen 10 mg mane led to a gradual subjective and functional improvement. The skin felt progressively softer, and cellulitis became an ever-decreasing problem. Whilst abdominal girth reduced, lower limb volumes remained basically unchanged. However, hip and knee flexion improved and there was marked increase in his exercise tolerance.

We lost track of the man after a year of careful follow up as he returned to an ever more active life, including a return to driving and to employment. He resumed contact a year later just prior to insertion of an inferior vena cava stent, which had been reconsidered due to the marked improvement in his functional status. It was noted at this time that his collateral cutaneous circulation was much less prominent even though inferior vena cava diameter was just 4 mm.

Thirty-two months after starting tamoxifen, he continues on this treatment without side effects. Lower limb volumes are basically unchanged but their shapes have improved significantly. He now has right knee flexion of 135 degrees and left knee flexion of 145 degrees. The skin is soft and supple and there has been just one episode of cellulitis in the last two years. The interval between ureteric stent changes has increased from six months to twelve months.

**Discussion**

Whilst the mechanism of action of tamoxifen in RF remains unexplained, the drug appears to have non-hormonal modes of action as well as well-recognised hormonal ones. For example, up to 10% oestrogen receptor negative breast cancers respond to tamoxifen therapy and a variety of non-hormonal mechanisms by which tamoxifen might reduce cellular proliferation have been postulated.\(^4,6\) Although the clinical response of RF to tamoxifen is typically slow, complete regression has been described. However, withdrawal of tamoxifen leads to clinical relapse that is reversed by reintroduction of the drug.\(^4\) Therefore long-term treatment is recommended. Our patient was started and maintained on an arbitrary low tamoxifen dose of 10 mg a day, but another case study described a patient with an improved response when an initial dose of 10 mg OD was increased to 40 mg OD.\(^6\) It therefore seems appropriate to titrate the dose upwards if a low starting dose proves ineffective. Low dose treatment with tamoxifen appears well tolerated, but cases of thrombocytopenia and steatohepatitis have been reported. Men taking tamoxifen for breast cancer have also reported impotence, reduced libido and mood swings.

RF is a rare condition that could be encountered occasionally in the hospice setting, particularly in lymphoedema patients. Several reports have described the successful use of tamoxifen in the management of ureteric obstruction secondary to RF. However, we believe this is the first published report of subjective and objective functional improvement in lymphoedema through the use of tamoxifen in a patient with RF, even though limb volumes remained essentially unchanged.

**References**


